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Original Article

Evaluation of antioxidant activity in without persistent ST-segment elevation

Mustafa Kaan Dişyapar[1], Şaban Keleşoglu[2], Ahmet Çınar[1], Özcan Erel[3], Salim Neşelioglu[3], Yücel Yılmaz[1]

[1]Department of Cardiology, Kayseri City Hospital, Kayseri Faculty of Medicine, University of Health Sciences, Kayseri, Turkey
[2]Department of Cardiology, Faculty of Medicine, Erciyes University, Kayseri, Turkey
[3]Department of Medical Biochemistry, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Turkey

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Corresponding Author: Yücel Yılmaz, dryyilmaz@hotmail.com

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ABSTRACT

Aims: Coronary artery disease is the most common cause of mortality and morbidity worldwide. Oxidative stress is involved in the pathogenesis of many diseases, including atherosclerosis. Thiols are important antioxidants for the elimination of reactive oxygen radicals and oxidative stress. In this study, we aimed to compare patients suffering from without persistent ST-segment elevation (NSTMI) and volunteers with normal coronary arteries in terms of antioxidants.

Methods: The study included 105 patients diagnosed with NSTMI and 51 controls. Plasma total thiol, native thiol, and disulfide levels were measured.

Results: Baseline demographic characteristics were similar between the groups. The ejection fraction was lower in the patient group. In terms of biochemical and hematologic parameters, glucose, AST, ALT, white blood cell count, and troponin were higher in the patient group, while other parameters were similar. Plasma native thiol (344.32±81.28 µmol/L versus 403.62±62.36 µmol/L, p<0.0001) and total thiol (382.90±91.13 µmol/L versus 444.17±65.53 µmol/L, p<0. 0001) levels were lower in NSTMI patients compared to control patients, while disulfide (19.29± 3.19 versus 20.27± 8.10, p=0.77) levels were similar between the groups.

Conclusion: In this study, we found that native thiol and total thiol levels, which are antioxidant markers, were lower in patients with NSTMI compared with the control group. Our study shows that antioxidant activity is affected in NSTMI, and antioxidant levels are decreased..

Keywords: Without persistent ST-segment elevation, thiol, antioxidant

INTRODUCTION

Cardiovascular disease also has a significant impact on global health. According to the World Health Organization, deaths from cardiovascular disease (CVD) represent 29% of all deaths, and deaths from CVD are increasing despite all advances in diagnosis and treatment.1 Ischemic heart disease is mostly caused by atherosclerotic plaques. Epicardial arterial stenoses that restrict coronary blood flow create an imbalance between myocardial oxygen supply and demand. Various pathological mechanisms are responsible for the formation of atherosclerosis and are seen as endothelial dysfunction, lipid penetration and deposition in the vascular intima, exaggerated adaptive immune responses, vascular smooth muscle cell proliferation, and remodeling of the extracellular matrix.[2]

Recent studies increasingly suggest that oxidative stress is also involved in the mechanism of atherosclerosis development.3-5 When oxidant stress occurs, it is thought to be involved in almost all steps of atherosclerotic plaque formation, including thrombus formation.[6,7]

Oxidant and antioxidant systems work together in a balance in the body. However, if this balance is disrupted in favor of oxidant substances, oxidative stress occurs. Free radicals formed due to increased oxidative stress play a role in the development and progression of atherosclerosis and facilitate the emergence of various CVS diseases.[8,9] Thiol groups are an antioxidant cascade that plays a vital role in the elimination of reactive oxygen species.[10,11] The components of antioxidants in this group that provide homeostasis are total thiol, natural thiol, disulfide, and organic compounds containing a sulfhydryl (-SH) group that react with oxidant molecules and neutralize them.[11,12]

Studies have shown that there is a relationship between antioxidant system levels and coronary artery disease (CAD).[8,10,11] In this study, we aimed to investigate antioxidant levels in patients suffering from without persistent ST-segment elevation (NSTMI).

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METHODS

Study Population

The study was initiated with the approval of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.03.2020, Decision No: 20). The study included patients admitted to the Cardiology Intensive Care Unit (CICU) of our hospital between April 2020 and November 2020. This study is a single-center and prospective study. The patients included in the study were 105 patients diagnosed with NONSTMI according to the European Society of Cardiology (ESC) criteria.[13] The control group consisted of 51 patients with similar baseline characteristics. The control group was selected from those who underwent coronary angiography and were found to have normal coronary arteries. The medical history of all participants, including cardiovascular risk factors and medications, was obtained and recorded. All patients underwent routine physical examinations and transthoracic echocardiography.

All patients underwent coronary angiography as an invasive emergency strategy and continued with percutaneous coronary intervention (PCI) when necessary. All patients received medical treatment regimens during hospitalization according to the current guidelines of the ESC.[13]

We excluded patients with previous coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), a history of acute coronary syndrome in the last 3 months, hematologic disease, malignancy, chronic renal failure or liver disease, and ongoing infection or chronic disease. Patients with inflammatory diseases, autoimmune diseases, or those taking vitamin supplements were also excluded. All patients gave written informed consent before study participation. The research protocol for this study, which complies with the Declaration of Helsinki, was approved by the local research ethics committee.

Laboratory Analysis

For laboratory examination, blood samples were collected from all patients between 8:00 a.m. and 10:00 a.m. following a 12-hour fast after CICU admission. Antecubital venous blood samples were transferred into tryptophan-EDTA based anticoagulated tubes. Blood samples were used to measure basic blood variables (a comprehensive metabolic panel and complete blood count) and thiol levels. All routine biochemical tests were also performed on an autoanalyzer (Roche Diagnostic Modular Systems, Tokyo, Japan). Hematological parameters were analyzed with a Sysmex K-1000 automated analyzer within 30 minutes of sample collection.

We measured the levels of thiol groups and thiol/disulfide homeostasis as described by Erel et al.[14] thiol samples were centrifuged at 1500 g for 10 minutes. We stored plasma at -80°C and processed all samples simultaneously. We detected serum natural thiol and total thiol levels spectrophotometrically. First, we measured serum natural thiol levels after a reaction with 5, 5'-dithiobis-2-nitrobenzoic acid (DTNB) without any treatment. Secondly, to measure total thiol levels, we reduced dynamic disulfide bonds in serum samples using sodium borohydride (NaBH4) to form free functional thiol groups. Then, we used formaldehyde to eradicate unused NaBH4 and measured total thiol groups, including both reduced and natural ones, following reaction with DTNB. We calculated the number of dynamic disulfide bonds by determining half the difference between total thiol and natural thiol.

Transthoracic Echocardiography

We performed transthoracic echocardiography on each participant in the CICU and the control group. We performed all measurements using a machine (Vivid 5, GE Medical System, Horten, Norway) with a 3.5 MHz transducer. We performed 2D echocardiographic measurements to assess left ventricular ejection fraction and valvular pathologies. We used Simpson's method and color Doppler echocardiography to assess ejection fraction and valvular pathologies in the apical 4-chamber view, respectively.

Statistical Analysis

All analyses were performed using SPSS V21.0 for Windows (version 21.0; SPSS, Chicago, Illinois). All data are presented as mean±standard deviation unless otherwise stated. The Kolmogorov-Smirnov test was used to analyze the distribution pattern. A comparison of parametric values between two groups was performed using the independent samples t-test. A comparison of nonparametric values between the two groups was performed using the Mann-Whitney U test. The distribution of continuous variables between groups was performed with one-way ANOVA. Variability between groups was measured via the LSD test. Categorical variables were compared with the chi-square test. A P value<0.05 was considered significant.

RESULTS

Baseline clinical and demographic characteristics of the study groups are presented in Table 1. There were no statistically significant differences between the patient and control groups in terms of age, smoking status, diabetes, and hypertension (p> 0.05). Systolic-diastolic blood pressures and basal heart rates were similar. In terms of echocardiography, EF was significantly lower in the patient group (p<0001).

In laboratory analysis, leukocyte (WBC), AST, ALT, and glucose levels were significantly higher in the patient group, while there was no significant difference between the groups in terms of other biochemical and hematologic values (Table 2).

Table 1: Basal characteristic, biochemical, and hematological parameters between groups

	NONSTMI (n=105)	Control Group (n=51)	p
Age	61.2±11.4	63.1 ±9.9	.541
Hypertension, n (%)	49 (%47)	23 (%45)	.644
Diabetes mellitus, n (%)	32 (%30)	14 (%27)	.625
Hyperlipidemia, n (%)	42 (%40)	19 (%37)	.925
Smoking, n (%)	48 (%46)	25 (%25)	.764
Systolic blood pressure (mmHg)	129.5±16.2	135.1±18.1	.622
Diastolic blood pressure (mmHg)	71.3±13.8	74.2±14.6	.329
Heart rate	88.1±12.4	76.3±10.5	.572
LVEF (%)	49.2±7.5	66±10.24	.0001*

Data are expressed as the mean±standard deviation for normally distributed data. NONSTMI: Without persistent ST-segment elevation, LVEF: Left ventricular ejection fractions, *p <0.05

When plasma thiol groups were evaluated, plasma native thiol (344.32±81.28 µmol/L versus 403.62±62.36 µmol/L, p<0.0001) and total thiol (382.90±91.13 µmol/L versus 444.17±65.53 µmol/L, p<0. 0001) levels were significantly lower in the patient group, whereas there was no significant difference between the groups in terms of disulfide levels (19.29±3.19 versus 20.27±8.10, p=0.77). Troponin I level (0.006-27 mg/dL, P<.001) was higher in the patient group (Table 2).

Table 2. Relationship between thiol and disulfide between groups

Variables	NONSTMI (n=105)	Control Group (n=51)	p
Native thiol (µmol / L)	344.32±81.28	403.62±62.36	.0001*
Total thiol (µmol / L)	382.90±91.13	444.17±65.53	.0001*
Disulfide	19.29± 3.19	20.27±8.10	.77
Glycose (mg/dl)	155.2±72.4	128,8±55.7	.0001*
GFR (mg/dk/1.732)	92±21.54	95.2±22.3	.342
AST (U/L)	41.4±16.2	27.2±1.9	.0001*
ALT (U/L)	32.1±13.1	24.4±12.6	.001*
Total cholesterol (mg/dl)	191±26.8	188±52.1	.467
Triglyceride (mg/dl)	171.54±66.7	169.5±81.3	.625
HDL (mg/dl)	39.5±12.1	42.1±14.5	.875
LDL(mg/dl)	121±42.1	119.2±41.9	.345
HBA1C (%)	7.5±3.1	7.6±1.8	.117
WBC (103/ µL)	13.1±3.6	9.1 ±3.6	.0001*
Hemogram (mg/dL)	14±2.1	14.2±1.5	.325
Platelets (103/ µL)	265.6±81.5	271.5±79.5	.673
Troponin I (mg/dL)	35	0.01	.001*

Data are expressed as the mean±standard deviation for normally distributed data. LDL: Low density lipoprotein, HDL: High density lipoprotein, WBC: White blood cell, AST: Aspartate amino transferase, ALT: Alanine amino transferase, NONSTMI: Without persistent ST-segment elevation, *p <0.05

CONCLUSION

To the best of our knowledge, this is the first study to investigate thiol/disulfide homeostasis as a marker of oxidative stress in NONSTMI patients, and it was shown to be decreased in this patient group.

The balance between oxidants and antioxidants is important for the healthy functioning of the body. Oxidants (reactive oxygen species (ROS)), which are products of cellular metabolism, can occur in the intracellular or extracellular environment.[15-17] Antioxidant defense systems such as superoxide enzymes (dismutase, glutathione peroxidase, catalase) and non-enzyme molecules (albumin, bilirubin, glutathione) are needed to maintain the oxidant-antioxidant balance.[18,19] When oxidants are produced in large amounts or cannot be eliminated by antioxidants, cells are exposed to active ROS.[18,20-22] Oxidative stress causes damage in many cells, including endothelial cells, and this is considered as the first stage of atherosclerosis.[23,24]

Thiols are sulfur analogs of alcohols, and disulfides are structures containing adjacent pairs of sulfur atoms.[25,26] The role of thiol/disulfide balance in antioxidant reactions is crucial. In addition, thiols, which are the main components of intracellular and extracellular damage protection mechanisms, are non-enzymatic antioxidants. Plasma thiol groups reduce oxidative damage in the pathophysiology of inflammatory processes in diseases such as CAD, rheumatoid arthritis, and diabetes mellitus.[27,28] In our study, thiol and disulfide values and ratios, which are members of the antioxidant system, were significantly lower in NOSTMI patients. This finding suggests that the antioxidant system was utilized in the patient group, and therefore its level decreased.

Studies demonstrating the relationship between plasma thiol levels, the thiol/disulfide ratio, and CAD are limited in the literature. Altıparmak et al.[10] showed that the disulfide/thiol ratio did not change significantly, but decreased native thiol levels were associated with the presence and severity of CAD.[8] found that native thiol, total thiol, and disulfide levels were lower in AMI patients compared to controls.[29] suggested that thiol disulfide volume at admission was independently associated with the development of contrast-induced nephropathy (CIN) after PCI in patients with acute coronary syndrome. In our study, it was confirmed that native thiol, total thiol, and disulfide levels were decreased in patients admitted with a diagnosis of NONSTMI. These results suggest that the levels of thiol groups can be used as markers to evaluate NONSTMI. Further studies with a more significant number of patients are needed to confirm the results obtained.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.03.2020, Decision No: 20).

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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